RESEARCH LETTER

Myocarditis and Pericarditis After Vaccination for COVID-19

Rare cases of cardiac inflammation following SARS-CoV-2 vaccination have been reported.[1-4] We reviewed the clinical records of vaccine recipients to identify cases of postvaccination myocarditis or pericarditis.

Methods | Forty hospitals in Washington, Oregon, Montana, and Los Angeles County, California, that were part of the Providence health care system and used the same electronic medical record (EMR) were included. All patients with documented COVID-19 vaccinations administered inside the system or recorded in state registries at any time through May 25, 2021, were identified. Vaccinated patients who subsequently had emergency department or inpatient encounters with diagnoses of myocarditis, myopericarditis, or pericarditis were ascertained from EMRs (see eTables 1 and 2 in the Supplement for exclusions and definitions).

Supplemental content

The monthly rates of first-time hospital diagnoses (excluding patients with previous diagnoses in January 2018-January 2019) in January 2019 through January 2021 (prevaccine period) and February through May 2021 (vaccine period) were compared.

The Wilson method was used to calculate 95% confidence intervals for single proportions. Change in incidence between periods and 95% confidence intervals for incidence were assessed using an exact rate ratio test assuming Poisson distribution, with a 2-sided $P < .05$ defining statistical significance. R version 2021 statistical software (R Foundation) was used. The Providence institutional review board approved the study with a waiver of informed consent.

Results | Among 2 000 287 individuals receiving at least 1 COVID-19 vaccination, 58.9% were women, the median age was 57 years (interquartile range [IQR], 40-70 years), 76.5% received more than 1 dose, 52.6% received the BNT162b2 vaccine (Pfizer/BioNTech), 44.1% received the mRNA-1273 vaccine (Moderna), and 3.1% received the Ad26.COV2.S vaccine (Janssen/Johnson & Johnson). Twenty individuals had vaccine-related myocarditis (1.0 [95% CI, 0.61-1.54] per 100 000) and 37 had pericarditis (1.8 [95% CI, 1.30-2.55] per 100 000).

Myocarditis occurred a median of 3.5 days (IQR, 3.0-10.8 days) after vaccination (mRNA-1273 vaccine, 11 cases [55%]; BNT162b2 vaccine, 9 cases [45%]) (**Table**). Fifteen individuals (75%; 95% CI, 53%-89%) were male, and the median age was 36 years (IQR, 26-48 years). Four persons (20%; 95% CI, 8%-42%) developed symptoms after the first vaccination and 16 (80%; 95% CI, 58%-92%) developed symptoms after the second. Nineteen patients (95%; 95% CI, 76%-99%) were

Table. Characteristics of Post–COVID-19 Vaccination Myocarditis and Pericarditis Cases[a]

Characteristics	Myocarditis (n = 20)	Pericarditis without myocarditis (n = 37)
Immunizations at symptom onset		
1	4 (20)	15 (40.5)
2	16 (80)	22 (59.5)
Vaccine received most recently before symptom onset		
Ad26.COV2.S	0	2 (5.4)
mRNA-1273	11 (55)	12 (32.4)
BNT162b2	9 (45)	23 (62.2)
Time from most recent immunization to symptom onset, median (IQR), d	3.5 (3-10.8)	20 (6-41)
Age, median (IQR), y	36 (26.3-48.3)	59 (46-69)
Sex		
Female	5 (25)	10 (27)
Male	15 (75)	27 (73)
Race and ethnicity[b]		
White	19 (95)	31 (83.8)
Asian	0	2 (5.4)
Latinx	0	2 (5.4)
Black	0	0
Other	0	2 (5.4)
Unknown	1 (5)	0
Encounter state		
California	1 (5)	7 (18.9)
Montana	0	1 (2.7)
Oregon	8 (40)	8 (21.6)
Washington	11 (55)	21 (56.8)
Comorbidities		
Alcohol or drug dependence	4 (20)	5 (13.5)
Coronary artery disease	1 (5)	4 (10.8)
Cancer	2 (10)	5 (13.5)
Heart failure	0	2 (5.4)
Cirrhosis	0	1 (2.7)
Chronic kidney disease	1 (5)	4 (10.8)
COPD	0	4 (10.8)
Diabetes	2 (10)	4 (10.8)
Hypertension	5 (25)	18 (48.6)
Autoimmune disease	0	3 (8.1)
Case management		
Admitted to hospital	19 (95)	13 (35.1)
Intensive care unit stay	2 (10)	1 (2.7)
Treated for heart failure[c]	8 (40)	5 (13.5)
Colchicine	9 (45)	20 (54.1)
NSAIDs	15 (75)	18 (48.6)
Systemic steroids	0	4 (10.8)
Length of stay, median (IQR), d	2 (2-3)	1 (1-2)

(continued)

Table. Characteristics of Post–COVID-19 Vaccination Myocarditis and Pericarditis Cases[a] (continued)

Characteristics	Myocarditis (n = 20)	Pericarditis without myocarditis (n = 37)
Laboratory findings (highest value during hospital visit)		
ALT ≥50 U/L	1 (5)	2 (5.4)
AST ≥50 U/L	6 (30)	1 (2.7)
Creatinine ≥1.2 mg/dL	1 (5)	4 (10.8)
Hemoglobin <9 g/dL	0	0
White blood cell count ≥12 000/μL	3 (15)	8 (21.6)
Absolute neutrophils, median (IQR), $\times 10^9$/L	5 (3.5-7.5)	7 (5-8)
Absolute lymphocytes, median (IQR), $\times 10^9$/L	2 (1.5-2)	2 (1-2)
Platelets $<100\times 10^3$/μL	0	0
Platelets $\geq 400\times 10^3$/μL	0	2 (5.4)
ESR ≥30 mm/h	0	5 (13.5)
Elevated troponin level	19 (95)	0
Temperature ≥38 °C	0	0
Bundle branch block	1 (5)	2 (5.4)
ST elevation	9 (45)	14 (37.8)
PR depression	0	7 (18.9)
Corrected QT interval, median (IQR), ms	444 (425-467)	425 (413-457)
Ejection fraction <50%	5 (25)	3 (8.1)
Clinical status at last follow-up		
Resolved	13 (65)	7 (18.9)
Improved	7 (35)	23 (62.2)
Persistent	0	2 (5.4)
Insufficient documentation	0	5 (13.5)
Time from symptom onset to last follow-up, median (IQR), d	23.5 (4.8-41.3)	28 (7-53)
Returned to hospital for same symptoms	1 (5)	1 (2.7)
Died	0	0

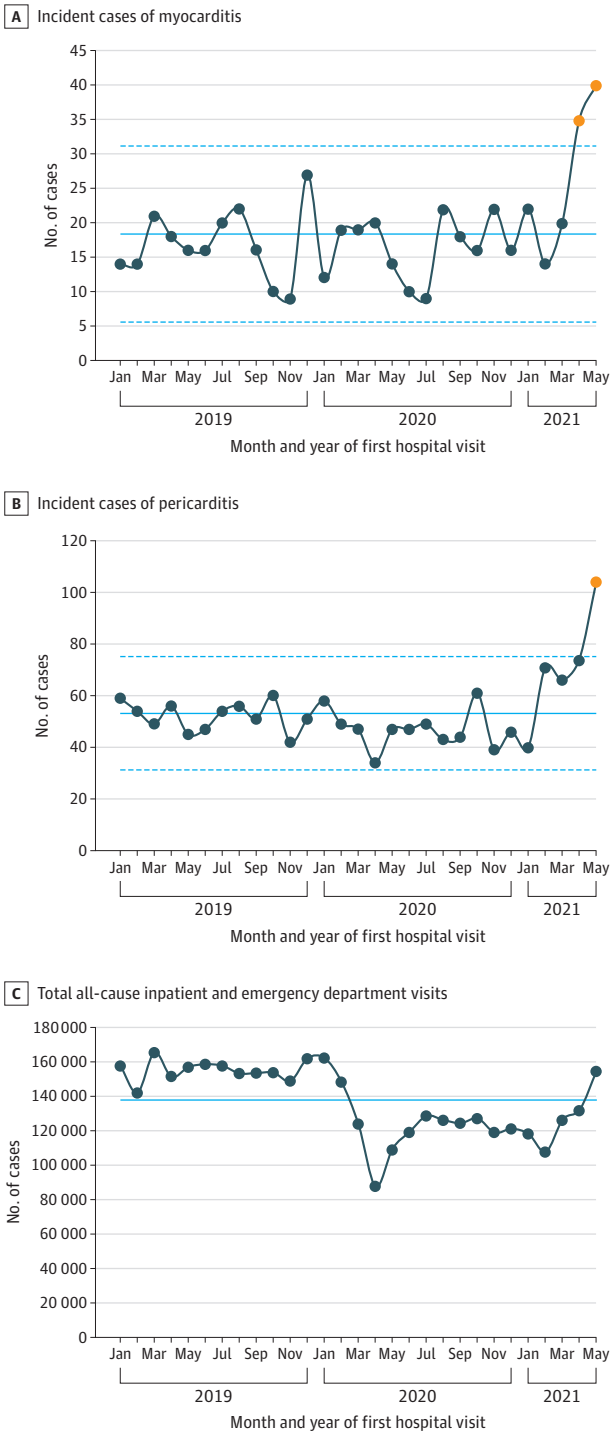
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; COPD, chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; IQR, interquartile range; NSAID, nonsteroidal anti-inflammatory drug.

[a] Data are No. (%) of patients unless otherwise specified.

[b] Race and ethnicity information was obtained from electronic medical records, where this information is assigned by either patients or health care registration personnel; these data are reported owing to the possibility of racial and ethnic differences in rates of postvaccination myocarditis and/or pericarditis.

[c] Treated with diuretics, β-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers.

Figure. Monthly Number of Inpatient and Emergency Department Cases of Myocarditis and Pericarditis at 40 Hospitals in the Western US



A statistical process control c-chart was used for panels A and B, with control limits at ±3 times the standard deviation of the overall count. Orange circles are counts outside the control limits. Solid lines are incidence over the entire time frame; dashed lines are the ±3 sigma (control limits) about the incidence over the entire time frame.

admitted to the hospital. All were discharged after a median of 2 days (IQR, 2-3 days). There were no readmissions or deaths. Two patients received a second vaccination after onset of myocarditis; neither had worsening of symptoms. At last available follow-up (median, 23.5 days [IQR, 4.8-41.3 days] after symptom onset), 13 patients (65%; 95% CI, 43%-82%) had symptom resolution and 7 (35%; 95% CI, 18%-57%) were improving.

Pericarditis developed after the first immunization in 15 cases (40.5%; 95% CI, 26%-57%) and after the second immunization in 22 cases (59.5%; 95% CI, 44%-74%) (mRNA-1273 vaccine, 12 cases [32%]; BNT162b2 vaccine, 23 cases [62%]; Ad26.COV2.S vaccine, 2 cases [5%]). Median onset was 20 days (IQR, 6.0-41.0 days) after the most recent vaccination.

Twenty-seven individuals (73%; 95% CI, 57%-85%) were male, and the median age was 59 years (IQR, 46-69 years). Thirteen (35%; 95% CI, 22%-51%) were admitted to the hospital, none to intensive care. Median stay was 1 day (IQR, 1-2 days). Seven patients with pericarditis received a second vaccination. No patient died. At last available follow-up (median, 28 days; IQR, 7-53 days), 7 patients (19%; 95% CI, 9%-34%) had resolved symptoms and 23 (62%; 95% CI, 46%-76%) were improving.

The mean monthly number of cases of myocarditis or myopericarditis during the prevaccine period was 16.9 (95% CI, 15.3-18.6) vs 27.3 (95% CI, 22.4-32.9) during the vaccine period ($P < .001$) (**Figure**). The mean numbers of pericarditis cases during the same periods were 49.1 (95% CI, 46.4-51.9) and 78.8 (95% CI, 70.3-87.9), respectively ($P < .001$).

Discussion | Two distinct self-limited syndromes, myocarditis and pericarditis, were observed after COVID-19 vaccination. Myocarditis developed rapidly in younger patients, mostly after the second vaccination. Pericarditis affected older patients later, after either the first or second dose.

Some vaccines are associated with myocarditis,[5] including mRNA vaccines,[1-4] and the Centers for Disease Control and Prevention recently reported a possible association between COVID-19 mRNA vaccines and myocarditis, primarily in younger male individuals within a few days after the second vaccination, at an incidence of about 4.8 cases per 1 million.[6] This study shows a similar pattern, although at higher incidence, suggesting vaccine adverse event underreporting. Additionally, pericarditis may be more common than myocarditis among older patients.

Study limitations include cases missed in outside care settings and missed diagnoses of myocarditis or pericarditis (which would underestimate the incidence), as well as inaccurate EMR vaccination information. Temporal association does not prove causation, although the short span between vaccination and myocarditis onset and the elevated incidence of myocarditis and pericarditis in the study hospitals lend support to a possible relationship.

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Accepted for Publication: July 26, 2021.

Published Online: August 4, 2021. doi:10.1001/jama.2021.13443

Author Contributions: Dr Robicsek had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Diaz, Robicsek.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Diaz, Parsons, Meier, Hutchinson, Robicsek.
Critical revision of the manuscript for important intellectual content: Diaz, Gering, Hutchinson, Robicsek.
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Administrative, technical, or material support: Parsons, Gering, Robicsek.
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Conflict of Interest Disclosures: Dr Diaz reported receipt of clinical trial research support from Gilead Sciences, Regeneron, Roche, Boehringer Ingelheim, and Edesa Biotech and scientific advisory board membership for Safeology. No other disclosures were reported.

Additional Contributions: We acknowledge the patients included in this study and the caregiver teams across the Providence organization.

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COMMENT & RESPONSE

Association of Coronary Artery Bypass Grafting vs Percutaneous Coronary Intervention With Memory Decline in Older Adults

To the Editor The recent study by Dr Whitlock and colleagues[1] suggested that the rate of memory decline at 5-year follow-up did not differ significantly among older adults undergoing coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). However, we have some concerns about this study.

First, the authors failed to describe whether the patients undergoing PCI had ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI). As previously demonstrated, STEMIs are more frequently associated with cardiogenic shock and poor peripheral perfusion, which may be responsible for about 30% of postprocedural asymptomatic brain infarction.[2] Second, increased PCI procedural complexity and longer procedural time are predictors of asymptomatic brain infarction[3] and may potentially affect future memory decline. Therefore, PCI procedural complexity and procedural time should be considered as potential confounding factors. Third, the access used during PCI, which was not described in this study, may have an effect on future memory impairment because radial access has